

**REMARKS**

Claims 1-65 were pending in the application. Claims 1, 11, 19, 20, 21, 23, 25, 28, 34, 39-41, 47-49, 56, 57, and 62 have been amended. Accordingly, after the amendments presented herein have been entered, claims 1-65 will remain pending.

No new matter has been added. Support for the amendments to the claims may be found throughout the specification and claims as originally filed. Specifically, claims 11, 19, 21, 34, 40, 41, 47, 56, and 57 were amended to correct informalities such as grammatical errors and repeated phrases. Claims 25 and 39 were amended to provide proper dependency. Support for the amendments to claim 1 can be found, for example, at least at page 7, lines 5-11 and at page 15, lines 15-18 of the specification as originally filed. Support for the amendments to claim 11, can be found, for example, at least at page 7, line 37, through page 8, line 1, of the specification as originally filed. Support for the amendments to claim 20 can be found, for example, at page 15, lines 15-18 of the specification as originally filed. Support for the amendments to claims 23 and 28 can be found, for example, at least in original claim 20, and at page 9, lines 25-28 of the specification as originally filed. Support for the amendments to claim 48 can be found, for example, at least at page 27, lines 4-5 of the specification as originally filed. Support for the amendments to claim 49 can be found, for example, at least in original claim 48 and at page 27, lines 17-21, of the specification as originally filed. Support for the amendments to claim 62 can be found, for example, at least at page 7, lines 5-11, of the specification as originally filed.

Cancellation of and/or amendments to the claims as originally filed should in no way be construed as an acquiescence to any of the rejections/objections set forth in the instant Office Action, and were made solely to expedite prosecution of the above-identified application. Applicants reserve the right to pursue the claims as originally filed, or similar claims, in one or more patent applications.

***Objections to the Disclosure***

At paragraph 4 of the pending Office Action, the Examiner has objected to the disclosure and has requested that the status of the parent application at page 1, line 9, of the specification be updated. The Examiner has also requested that the paragraph at page 15, lines 3-13, and the

Tables at page 61 of the specification be amended in order to reflect the new sequence identifiers.

Applicants have amended the specification as requested by the Examiner, thereby rendering the aforementioned objections moot. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw these objections to the disclosure.

***Objections to Claims 11-14, 19, 21, 34, 39, 40, 41, 47, 56, and 57***

At paragraph 5 of the pending Office Action, the Examiner has objected to claims 11-14, 19, 21, 34, 39, 40, 41, 47, 56, and 57. In particular, the Examiner asserts that

[a]t claim 11, lines 2 and 3, “substituted or unsubstituted azacycloalkyl” is repeated. Claims 19, 34, and 41 do not end with periods. At claim 21, line 1, the second occurrence of “Z is” should be deleted. At claim 40, las line, the end parenthesis after “amino” is unmatched. At claim 47, line 1, and claim 56, line 1, “the a” should be changed to “a”. At claim 57, page 80, line 31, the beginning parenthesis before “3-“ does not match the end bracket after “enyl”. At claim 57, page 81, lines 1-23, the ID#’s should be not occur in the middle of the compound names.

At paragraph 6 of the pending Office Action, the Examiner has also objected to claim 39 indicating that “dependent claim 39 recites that D can be a cyclic C<sub>1-6</sub> alkyl. However, claim 34, upon which claim 39 depends, does not indicate that D can be a cyclic alkyl.”

Applicants submit that the aforementioned objections to the claims have been rendered moot in view of the amendments to the claims present herein. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw these objections to the claims.

***Rejection of Claims 23, 24, 28, 29, 49, 50, and 58-61 Under the Statutory Type (35 U.S.C. §101) Double Patenting***

The Examiner has rejected claims 23, 24, 28, 29, 49, 50, and 58-61 under 35 U.S.C §101 as “claiming the same invention as that of claims 4, 5, 9, 10, 30, 31, and 39-42 of prior U.S. Patent No. 6,548,477 (hereinafter the ‘477 patent) .

While in no way admitting that claims 23, 24, 28, 29, 49, 50 are the same or obvious over claims 4, 5, 9, 10, 30, 31 of the '477 patent, Applicants respectfully submit that the forgoing rejection of claims 23, 24, 28, 29, 49, and 50 has been rendered moot in view of the amendments to the claims. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw this rejection as it pertains to claims 23, 24, 28, 29, 49, and 50.

With respect to claims 58-61, Applicants respectfully traverse the rejection under 35 U.S.C. §101 as it pertains to these claims for the following reasons. Claim 58 includes the limitation that when P is hydrogen or -OR, Q is not hydrogen. Accordingly, claim 58 in the instant application is different from the corresponding claim 39 in the '477 patent. The same holds true for the dependent claims 58-61. In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw this rejection as it pertains to claims 58-61.

***Provisional Rejection of Claims 1-65 Under the Statutory Type (35 U.S.C. §101) Double Patenting***

The Examiner has provisionally rejected claims 1-65 under 35 U.S.C. §101 as "claiming the same invention as that of claims 1-61 and 64-67 of co-pending Application No. 10/429,174."

While in no way admitting that claims 1-65 are the same or obvious over claims 1-61 and 64-67 of co-pending Application No. 10/429,174, upon allowance of either the present application or the '174 application, Applicants will consider canceling or amending the conflicting claims, if appropriate, which will obviate this rejection.

***Rejection of Claims 1-10, 20-22, 25-27, 30-48, 51-57, and 62-65 Under the Doctrine of Obviousness Double Patenting***

The Examiner has rejected claims 1-10, 20-22, 25-27, 30-48, 51-57, and 62-65 under the judicially created doctrine of obvious type double patenting as "being unpatentable over claims 1-52 of U.S. Patent No. 6, 548,477." In particular, the Examiner is of the opinion that "[a]lthough the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '477 patent anticipate the instant claims".

Applicants respectfully submit that, while in no way admitting that the present claims are obvious over claims 1-52 of U.S. Patent 6,548,477, upon allowance of the present claims, Applicants will consider submitting a terminal disclaimer in compliance with 37 C.F.R. 1.321(b) and (c), if appropriate, which will obviate the rejection.

***Provisional Rejection of Claims 1-10 and 20-65 Under the Doctrine of Obviousness Double Patenting***

The Examiner has provisionally rejected claims 1-10 and 20-65 under the judicially created doctrine of obviousness-type double patenting as “being unpatentable over claims 1-43, 45-48, and 50-61 of co-pending Application No. 09/972,772.” The Examiner is of the opinion that “[a]lthough the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the ‘722 application anticipate the instant claims.”

Applicants respectfully submit that, while in no way admitting that the present claims are obvious over claims 1-43, 45-48 and 50-61 of co-pending Application No. 09/972,772, upon allowance of the ‘772 application, Applicants will consider submitting a terminal disclaimer in compliance with 37 C.F.R. 1.321(b) and (c), if appropriate, which will obviate the rejection.

***Provisional Rejections of Claims 1-10, 20-58, 61, 62, and 65 Under the Doctrine of Obviousness Double Patenting***

The Examiner has provisionally rejected claims 1-10, 20-58, 61, 62, and 65 under the judicially created doctrine of obviousness-type double patenting as “being unpatentable over claims 20-58, 60, 62, 71, and 74-84 of copending Application No. 10/138,935.” The Examiner is of the opinion that “[a]lthough the conflicting claims are not identically, they are not patentably distinct from each other because the claims of the ‘935 application anticipate the instant claims.” Further, the Examiner states that claims 1-10, 20-58, 61, 62, and 65 are “directed to an invention not patentably distinct from claims 20-58, 60, 62, 71, and 74-84 of commonly assigned copending Application No. 10/138,935.”

Applicants respectfully submit that while in no way admitting that the present claims are obvious over claims 20-58, 60, 62, 71, and 74-84 of co-pending Application No. 10/138,935,

upon allowance of the ‘935 application, Applicants will consider submitting a terminal disclaimer in compliance with 37 C.F.R. 1.321(b) and (c), if appropriate, which will obviate the rejection.

***Provisional Rejections of Claims 1-10, 20-59, 61-63, and 65 Under the Doctrine of Obviousness Double Patenting***

The Examiner has provisionally rejected claims 1-10, 20-59, 61-63, and 65 under the judicially created doctrine of obviousness-type double patenting as “being unpatentable over claims 74-132 of copending Application No. 10/962,333.” The Examiner is of the opinion that “[a]lthough the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the ‘333 application anticipate the instant claims.”

Applicants respectfully submit that while in no way admitting that the present claims are obvious over claims 74-132 of co-pending Application No. 10/962,333, upon allowance of the ‘333 application, Applicants will consider submitting a terminal disclaimer in compliance with 37 C.F.R. 1.321(b) and (c), if appropriate, which will obviate the rejection.

***Rejection of Claims 1-10, 57, and 62-65 Under 35 U.S.C. §102(e)***

The Examiner has rejected claims 1-10, 57, and 62-65 under 35 U.S.C. §102(e) as being anticipated by U.S. Patent No. 6,548,477 (hereinafter “the ‘477 patent”). The Examiner has further rejected claims 1-10, 57, and 62-65 under 35 U.S.C. §102(e) as being anticipated by U.S. Patent Application Publication 2002/0193298 (hereinafter “the ‘298 publication”).

While in no way acquiescing that the ‘477 patent and the ‘298 publication constitute proper 102(e) prior art against the claimed invention, Applicants would like to make the following remarks of record.

Applicants respectfully traverse these rejections. For prior art references to anticipate a claimed invention in terms of 35 U.S.C. §102, the prior art must teach ***each and every element*** of the claimed invention. Lewmar Marine v. Barent, 827 F.2<sup>nd</sup> 744, 3 USPQ2nd 1766 (Fed. Cir. 1987).

As amended, claims 1 and 62, and claims dependent therefrom, are directed to compounds of Formula I, wherein R<sub>3</sub> and R<sub>4</sub> are each, independently, substituted alkyl, substituted aryl, or substituted or unsubstituted heteroaryl; or R<sub>3</sub> and R<sub>4</sub> together with the carbon atom to which they are attached, form a carbocyclic or heterocyclic group; or R<sub>3</sub> or R<sub>4</sub> together form an alkylene group.

The '477 patent and the '298 publication do not teach or suggest such compounds. Rather, the '477 patent and the '298 publication teach compounds in which Q is a linear, branched or cyclic alkyl or aryl. Furthermore, the '477 patent and the '298 publication do not teach or suggest the specific compounds recited in amended claim 57. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-10, 57, and 62-65 under 35 U.S.C §102(e).

***Rejection of Claims 1, 7, 8, 20, 25-27, 30-37, and 42 Under U.S.C. §102(b)***

The Examiner has rejected claims 1, 7, 8, 20, 25-27, 30-37, and 42 under 35 U.S.C § 102(b) as being anticipated by Griffith *et al.* (1998) *Proc. Natl. Acad. Sci.* 95:15183-15188. In particular, the Examiner is of the opinion that the Griffith *et al.* article teaches compound 8 in Figure 2B which corresponds to Applicants' compound of formula (XV) and formula I. The Examiner further states that “[t]he examiner assumes that Applicants' claims do not exclude the possibility that the P group may be modified at its N-terminus, e.g., by a group corresponding to the fluorescein group of the Griffith *et al* article's compound 8.”

Applicants respectfully traverse this rejection for the following reasons. For prior art references to anticipate a claimed invention in terms of 35 U.S.C §102, the prior art must teach *each and every element* of the claimed invention. Lewmar Marine v. Barient, 827 F.2<sup>nd</sup> 744, 3 USPQ2nd 1766 (Fed. Cir. 1987).

As amended, claims 1 and 20, and the claims that depend therefrom, are directed to compounds in which the N-terminus of the peptide can be -NR<sub>2</sub>R<sub>3</sub>, wherein R<sub>2</sub> is hydrogen, alkyl or arylalkyl and R<sub>3</sub> is hydrogen, alkyl, arylalkyl or acyl. Griffith *et al.* do not teach or suggest such compounds. Therefore, Applicants respectfully request that the Examiner reconsider and withdraw this rejection of the claims.

***Rejection of Claims 1, 7, 8, 62 and 63 Under U.S.C. §102(b)***

The Examiner has rejected claims 1, 7, 8, 62, and 63 under 35 U.S.C. §102(b) as being anticipated by Folkman *et al.* (U.S. Patent No. 6,017,954) [hereinafter “the ‘954 patent”]. The Examiner indicates that the ‘954 patent “teaches a compound in Example 28 which is used to treat angiogenic diseases” and that “[t]he compound of Example 28 corresponds to Applicants’ compound of Formula I in which...Z is NR<sub>8</sub>, and R<sub>8</sub> is methyl...and P is methyl.”

Applicants respectfully traverse this rejection. For prior art references to anticipate a claimed invention in terms of 35 U.S.C. §102, the prior art must teach *each and every element* of the claimed invention. Lewmar Marine v. Barent, 827 F.2<sup>nd</sup> 744, 3 USPQ2nd 1766 (Fed. Cir. 1987).

Claims 1 and 62, as amended, and the claims dependent therefrom, are directed to compounds in which P is hydrogen or a peptide consisting of from 1 to about 100 amino acid residues attached at its carboxy terminus to Z. The ‘954 patent does not teach or suggest such compounds. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw this rejection of the claims.

***Rejection of Claim 64 Under 35 U.S.C. §103(a)***

The Examiner has rejected claim 64 under 35 U.S.C. §103(a) as being obvious over Folkman *et al.* (U.S. Patent No. 6,017,954) as applied against claims 1, 7, 8, 62, and 63, and further in view of Yanai *et al.* (U.S. Patent No. 5,422,363) [hereinafter “the ‘393 patent”] or Folkman *et al.* (U.S. Patent No. 6,086, 865) [hereinafter “the ‘865 patent”]. The Examiner indicates that the ‘954 patent teaches that the compounds can be administered to treat angiogenic diseases, but does not specifically teach the treatment of rheumatoid arthritis. Further, the Examiner indicates that the ‘363 patent and the ‘865 patent teach the administration of fumagillo derivatives to treat diseases associated with angiogenesis, such as rheumatoid arthritis. Specifically, the Examiner states that

[i]t would have been obvious to one of ordinary skill in the art at the time Applicants’ invention was made to administer the compounds of Folkman et al ‘954 so as to treat rheumatoid arthritis, because the compounds of Folkman et al ‘954 are disclosed to be useful in treating angiogenic diseases in general, and

because Yanai et al and Folkman et al '865 teach that rheumatoid arthritis is an angiogenic disease treatable by similar fumagillo derivatives.

Applicants respectfully traverse this rejection for the following reasons. To establish a *prima facie* case of obviousness, it is necessary for the Examiner to present evidence, preferably in the form of some teaching, suggestion, incentive or inference in the applied references, or in the form of generally available knowledge, that one having ordinary skill in the art would have been motivated to make the claimed invention and would have had a reasonable expectation of success in making the claimed invention. Under section 103, "[b]oth the suggestion and the expectation of success must be founded in the prior art, not in applicant's disclosure" (Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd. 927 F.2d 1200, 1207, 18 USPQ2d 1016 (Fed. Cir. 1991), quoting *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed Cir. 1988)). Moreover, when a combination of references are used to establish a *prima facie* case of obviousness, the Examiner must present evidence that one having ordinary skill in the art would have been motivated to combine the teachings in the applied references in the proposed manner to arrive at the claimed invention. See, e.g., *Carella v. Starlight Archery*, 804 F.2d 135, 231 USPQ 644 (Fed. Cir. 1986); and *Ashland Oil, Inc. v. Delta Resins and Refractories, Inc.*, 776 F.2d 281, 227 USPQ 657 (Fed. Cir. 1985).

As discussed in more detail above, the '954 patent fails to teach or suggest the claimed compounds or methods of using the same. Moreover, the secondary references relied upon by the Examiner, namely, the '363 patent and the '865 patent, do not make up for the deficiencies of the primary reference in that they also fail to teach or suggest the claimed compounds, or methods of using the same.

In view of the foregoing, Applicants respectfully submit that the '954, the '363 and the '865 patents, alone or in combination, fail to render the claimed invention obvious. Therefore, Applicants request that the Examiner reconsider and withdraw this rejection of the claims.

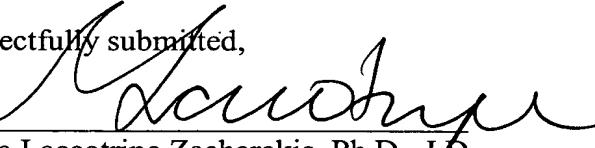
**CONCLUSION**

In view of the above amendments and remarks, Applicants believe that the pending application is in condition for allowance.

Applicants believe that no fee is due with this Amendment and Response. However, if a fee is due, please charge our Deposit Account No. 12-0080, under Order No. PPI-106CP2 from which the undersigned is authorized to draw.

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Respectfully submitted,

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